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NUCLEIN THERAPY

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NUCLEIN THERAPY

ITS RATIONALE, METHODS AND RESULTS



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REMEDIAL AGENT

THE SCOPE OF ITS APPLICATION CONSTANTLY WIDEN-
ING WITH INCREASED EXPERIENCE

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NUCLEIN THERAPY.

Unquestionably the trend of modern medicine is in the direction of rational, as distinguished from purely empirical, therapeutics. By rational therapeutics must be understood the employment of means suggested by the functional activities and resources of the human body, "the disease-resisting powers of the body." The efforts which nature makes to rid the body of disease, art may second and support; but in order that this co-operation may become effective, every theory with which the physiologist approaches his task must be tested in the fires of experience. Empiricism pure and simple is merely a partnership of conjecture and superstition, but empiricism in the service of science (in other words, intelligent experimentation) is indispensable to all permanent progress. Nuclein therapy is rational, supported by experimental evidence. Its very terminology is taken from nature, and its aim is nothing more or less than to furnish to the human organism directly what is constantly being acquired by a more circuitous process, in order that crises of inequality between supply and demand may be overcome and the balance turned in favor of the cells and tissues of the body.

Notwithstanding the many more or less successful efforts that had been made in the field of organo-therapy, it was still a most daring flight of imagination that first led to the examination of the blood-corpuscles for the purpose of discovering the substance which was believed to act as an antidote to disease, thus getting at once to the very root of self-cure and making the laboratory a recruiting office for the artificial increase of the "defensive proteids" of the patient. The theory that underlies serum therapy is less audacious, yet belonging to the same class; for while every toxin may have a specific antitoxin, the nucleins (or the white blood-corpuscles to which they are so closely related) are supposed to be the regular standing army of defense—they are not specific,

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but general; not local, but constitutional. The most patient and resourceful investigators in this field do not, however, dream of superseding the need of special remedies by the discovery of a panacea.

The *modus operandi* of natural resistance to disease is not yet, and probably never will be, fully understood; but that it belongs in part at least to the blood is proved by the presence in this fluid of a defensive or germicidal element, which bears a certain definite relation to the white blood-corpuses—is, in fact, believed to be secreted by these corpuscles, as it has been isolated from them by Drs. Vaughan and McClintock and others. But whether a natural secretion or an essential constituent, this germicidal substance—to which the name of NUCLEIN has been given—is demonstrably competent to cause leucocytosis, or multiplication of the white cells, when administered as a medicament. To be sure, the nuclein thus administered is a foreign product, isolated from yeast or other material, but its chemical reactions are the same as those of the natural product. Professor Kossel, of Berlin, has shown that a 0.5-per-cent. solution of nuclein is capable of speedily destroying cholera and typhoid bacilli; while clinical experience has already contributed a record which indicates that in many and widely divergent diseases the new remedy is worthy of confidence.

As to the richness of yeast in nuclein or some other remedial agent, it may be mentioned that Dr. Bracker, of Paris, in a paper recently read before the International Medical Congress at Rome, presented a series of observations on the treatment of certain infectious diseases by means of sterilized yeast cultures, the results having proved extremely favorable. "Yeast, or 'barm,' as an empirical remedy purely," says the *Medical Age*, "in days gone by won for itself golden opinions in typhoid, diphtheria, consumption, and other maladies." The reason why yeast is employed in the manufacture of our Nuclein is that it yields a greater quantity of pure nucleinic acid, more securely guarded from contamination with by-products, than any other substance known to us.

Our NUCLEIN SOLUTION, 5-PER-CENT., rendered perfectly

aseptic through costly and elaborate methods of purification, is adapted particularly for hypodermatic administration. NUCLEIN SOLUTION No. 2, also of 5-per-cent. strength, but not entirely isolated from albuminous matters, we supply for oral administration exclusively. The clinical reports contained in this brochure are for the most part based upon the employment of the more refined product; yet a number of practitioners who have employed Solution No. 2 assure us that the characteristic nuclein effects are produced when the remedy is administered by mouth. The leucocytosis seems to be just as pronounced (see table, page 12). Perhaps a better form than either of the above for continuous administration is gelatin capsules, each containing 2 grains of nucleinic acid, dry. The powder, like the nuclein in the solutions, is derived from yeast. Difficulties in manufacture for a long time prevented us from marketing NUCLEIN CAPSULES, but these difficulties are now overcome.

In the administration of nuclein, as of every other remedy, the purity of the medicament is a matter of prime importance. The distinguishing characteristic of the nucleins chemically is their richness in phosphorus, and a very simple test will demonstrate the utter worthlessness of most of the alleged "nuclein" offered in competition with our solution. Nucleinic acid is insoluble in dilute hydrochloric acid. Add one drop of the latter and a small amount of alcohol to a small quantity of our preparation, and the nucleinic acid will be thrown down in the form of a white flocculent precipitate. Other solutions on the market, similarly treated, will not respond to this test.

We have the authority of Dr. Charles T. McClintock, late of the Michigan University, for the statement that the hypodermatic exhibition of nuclein is a very simple and safe matter. After the patient has exposed the chest or back, one-half minute is ample time for disinfecting the skin, filling the syringe, and giving the injection. If, he adds, the syringe is once thoroughly disinfected, and if nothing but nuclein is used in it, it does not need any further care—that is, it will remain sterile indefinitely. For greater security,

however, an occasional ablution in 5-per-cent. carbolic acid, followed by rinsing in recently boiled water, is desirable. In the Doctor's own practice the nuclein solution is placed in a glass dish about two inches in diameter and half an inch in depth, which has been sterilized by heat; during office hours the nuclein remains in the open dish; afterwards the dish and syringe are placed in a covered glass receptacle, and are ready for use the next morning without any treatment whatever. Of course, if the solution is only used semi-occasionally, it would be advisable to protect it from evaporation and possible contamination. In the many thousands of nuclein injections made by Dr. McClintock, no serious result has ever occurred. When not in use, the needle is submerged in carbolic solution, which should be changed every two weeks.

The above is but to say that the idea that the hypodermatic administration of nuclein is difficult or dangerous is entirely without foundation. It is far easier to give a hypodermatic injection of nuclein than one of morphine, not having to dissolve tablets, etc., and with not one-hundredth of the danger of abscesses or other complications.

In giving large quantities of liquid hypodermatically there is, of course, always more or less danger of induration and abscess; to avoid these, observe the following precautions:

Keep the syringe and needle aseptic, as suggested above.

Sterilize the site of the proposed injection by thoroughly washing with a 5-per-cent. carbolic solution: this disinfects the skin and also acts as a local anesthetic, diminishing the pain of the injection.

Do not pinch up a fold of the skin between thumb and finger, but press downward and outward, making the skin tense; thrust the needle in quite deeply, and inject slowly. Numbness of adjacent skin, which may run down the nearest arm or leg, occasionally follows the injection; it need occasion no alarm, and passes off in a few hours.

Begin with ten minimis, and gradually increase by five minimis a day, up to sixty or eighty minimis.

To get the nuclein into the syringe, it will be found con-

venient to have a small dish or beaker: a large salt-cellar will do. This should be sterilized in the same manner as the syringe. Pour into this small dish the amount of nuclein to be used, and then draw into the syringe.

Keep the syringe, needle, small dish, and bottle of nuclein in some dust-proof receptacle.

A syringe holding eighty minims is much more convenient than a smaller one that has to be refilled several times.

If nuclein (5-per-cent. solution) be administered internally, the dose should be half a teaspoonful to begin with, rapidly but guardedly increased to a teaspoonful, in a wineglass of water, three times a day (between meals and at bedtime). The stomach should not be burdened with digestive duties nor cumbered with the products of digestion when the nuclein is introduced.

In mouth and throat affections the solution can be used in any spray apparatus, or diluted with ten to fifteen volumes of water and used as a gargle.

Good results have followed the rectal injection of dilute solutions in cases of catarrhal and ulcerative conditions of the bowel.

Quinine and all the coal-tar antipyretics are to be avoided in the nuclein treatment; also atropine for night-sweats (Vaughan).

A warning note, sounded by Professor Vaughan in 1894, may be appropriately reproduced here. He said: "I am convinced, especially from my experiments on animals, that nucleinic acid, improperly used, may do harm. It acts by stimulating the organs that elaborate the polynuclear corpuscles, and these may be overstimulated. Nucleinic acid fails to be of service unless these cell-forming organs respond. They may fail to respond on account of lowered vitality, or they may be paralyzed, as it were, by an excessive dose of stimulant. The agent is not one to be used indiscriminately. Already some physicians are supplying tuberculous patients with hypodermic syringes and solutions of nucleinic acid, and telling them to go ahead and treat themselves. Such practice as this may make the study of this subject result in a misfortune."

The Working Hypothesis of Nuclein Therapy.

This is stated by Professor Vaughan (*Medical News*, Feb. 27, 1897), as follows:

1. The phagocytic theory of Metchnikoff, in so far as it teaches that the polynuclear white blood-corpuscles are active agents in preventing or retarding the multiplication of pathogenic germs in the body, is true.
2. The polynuclear corpuscles do not eat the bacilli, but they destroy the germ by virtue of the chemical action of some constituent or secretion.
3. The germicidal properties of blood-serum, demonstrated by the researches of Fodor, Nutall, Buchner and others, are due to a substance, or to substances, that originate in the polynuclear white blood-corpuscles.
4. The natural resistance of the body to bacterial disease will be strengthened by a physiological increase in the production of polynuclear white blood-corpuscles.
5. This increase in the polynuclear corpuscles may be induced by introducing into the animal the most distinctive constituent of these cells, which is nuclein.

The Increase of the Natural Capacity of Resistance by the Production of Hyperleucocytosis.

Dr. Martin Hahn, privatdozent of the Hygienic Institute of the University of Munich, has published (*Berliner Klin. Woch.*, Nov. 28, 1896) the results of some highly interesting investigations, which are summarized as follows in the January 1897 issue of *Medicine*:

Buchner demonstrated that immunity cannot be explained by simple phagocytosis, as exudates lose none of their bactericidal power when the leucocytes are killed by freezing.

* we do not deal with a phagocytic function of but with the decomposition or secretion

products of the leucocytes, which impart a greater bactericidal energy to exudates than is present in blood-serum.

These observations are significant in their bearing on the theory and practical treatment of infectious diseases. The fact that leucocytes, where they occur in great number, impart to the respective medium, presumably through the products of their secretion, a bactericidal energy, suggests that we may increase by artificial means the natural resistance of the human organism, which is identical with the bactericidal energy of the blood. Not every increase in the number of leucocytes possesses the same value in increasing the bactericidal action; the kind, origin, biological condition, etc., of the leucocytes are important factors.

Assuming that resistance is augmented by certain alexins, it would seem that the injection of these substances would be efficient; but it has been shown by Buchner that human resistance cannot be increased in this way, owing to the neutralizing antagonism of the alexins produced by different animals. Accordingly the writer has attempted the production of a hyperleucocytosis.

Unambiguous results were obtained only by experiments on dogs. The number of leucocytes in the arterial blood was determined, and the animals were then given subcutaneous injections of remedies stimulating leucocytosis. For this purpose albuminoids, such as albumose or nuclein, were employed, the latter in the form of a yeast nuclein solution, placed at the writer's disposal by the firm of Parke, Davis & Company. Good results were obtained from a nucleinic acid donated by the same firm. As large quantities of such preparations can be administered to the dog, it is easy to double the original number of the leucocytes in a short time. This is usually accompanied by a rise in temperature, varying according to the remedy used; in the dog it rarely exceeds 1 to $1\frac{1}{2}$ degrees. When the number of leucocytes has risen to double the normal, blood is withdrawn a second time. At first five to six hours elapsed before the second blood-letting; later an interval of twelve to fifteen hours was allowed to pass between the injection and the second bleeding.

The defibrinated blood, obtained in the stage of hyperleucocytosis, exerted a decidedly more energetic bactericidal effect than normal blood of the same animal; which would indicate that in dogs the course of infection may be very favorably influenced by artificial hyperleucocytosis.

A favorable action is to be expected from hyperleucocytosis only in those cases where the bacteria do not remain localized and cause mischief by their toxins, but where they really pass into the circulation. In the human subject, in harmony with the animal test, a decided increase is to be registered in the energy of the blood rich in leucocytes. The investigations are naturally not to be regarded as completed so far as the human subject is concerned. But in view of the results thus far obtained, it is highly probable that the bactericidal potency of human blood depends substantially on the number of leucocytes, and that it will be possible to augment the natural resisting power of the human subject through an induced hyperleucocytosis.

Of course, artificial hyperleucocytosis will not favorably influence all bacterial affections. With respect to diphtheria, it seems almost established that a persistent increase in the number of leucocytes is to be regarded as unfavorable—a fact which certainly calls for further explanation. In other infections, where the bacteria remain localized and exert their harmful action, not by their direct presence in the blood, but rather by their locally produced toxins, as in cholera and tetanus, but little is to be hoped for from hyperleucocytosis. Here we have less to do with the destruction of living bacteria than with the problem of immunizing the body against the toxins. In these conditions antitoxic serum therapy must continue to occupy the foreground of clinical interest. The situation is different in the septicemic infectious processes. The results thus far obtained in the treatment of anthrax by immunization with serum are by no means brilliant, despite varied and extended experiments. At all events, they are far inferior to those obtained from immunization through attenuated cultures. A similar state of things seems to prevail with respect to the strepto-

coccic serum. Accordingly, in those infectious processes which are due to the presence of bacteria in the blood, we have still left to us a field for immunization through attenuated cultures, and for cure through elevation of the natural powers of resistance. This cure is, prospectively, to be achieved through the artificial production of hyperleucocytosis.

The subjoined tables give the rate at which certain bacteria were destroyed by normal and leucocytic blood. The figures given express the percentage of germs remaining alive at the end of the respective periods:

1. Dog's blood. Staphylococcus pyogenes aureus:

	After two hours.	After five hours.
Normal blood.....	19.5	4
Leucocytic blood.....	2.9	1.7

2. Human blood. Bacterium coli:

Normal blood.....	41.1	7.5
Leucocytic blood.....	16.1	0.6

[The result of such experiments must be far-reaching. If we can with nuclein, as Hahn says, "easily double" the number of leucocytes, and presumably thus increase the power of the body to destroy invading disease germs, it means much for therapy.]

Relation of Nuclein Administration to Leucocytosis.

One of the first, if not the first, records made of the results of experiments upon animals and man to determine the effect of yeast nucleic acid upon the number of white blood-corpuses, is to be found in the Transactions of the Michigan State Medical Society for 1894. The experiments therein referred to were begun in 1892 by Dr. Huber, of Ann Arbor, under the direction of Professor Vaughan, who epitomizes them as follows:

"(1) The subcutaneous injection of nuclein increases the number of white blood-corpuses; (2) this increase occurs in

both healthy and tuberculous persons; (3) with like quantities of nuclein injected, the increase varies with the person—it may be slight and it may be three-fold; (4) this increase occurs principally in the polynuclear cells; (5) it is evident, as a rule, as soon as the third hour after treatment, and generally disappears by the forty-eighth hour.

The following details of one series of counts may be of interest:

Patient.	No. of white corpuscles per cubic millimeter before treatment.	No. of white corpuscles per cubic millimeter after treatment.	Total increase per cubic millimeter.	Per cent. of increase.	Interval between treatment and count.	Strength of nuclein—per cent.	Amount of solution used.	Method of administration.
Miss B	8421	12,395	3974	47+	3 h. 45 m.	1	1 <i>l</i>	h*
Miss F	7617	13,800	6249	52+	2 h. 45 m.	1	1 <i>l</i>	"
Miss H	4545	11,713	7188	158	4 h. 15 m.	1	"	"
Mrs. R	5000	11,578	6578	131+	3 h. 10 m.	1	"	"
Miss S	9333	14,084	4751	50-	2 h.	1	"	"
Mrs. D	9564	10,947	1383	14+	3 h.	5	3 <i>l</i>	m†
Miss M	5238	17,305	12,130	231+	2 h. 30 m.	5	3 <i>l</i>	"
Mr. M	7520	10,138	2613	34+	2 h. 30 m.	5	3 <i>l</i>	"
Miss A	5977	8533	2556	44+	2 h.	5	"	"
Mrs. N	8713	12,959	4246	48+	2 h. 30 m.	5	"	"
Miss S	8478	9189	711	8-	4 h.	5	3 <i>l</i>	"
Mrs. R	8441	8500	1059	12+	3 h.	5	3 <i>l</i>	"

* h—hypodermically.

† m—by mouth.

Von Mayer (*Deutsche Med. Woch.*, March 19, 1896), in the clinic of Professor von Jaksch, has made some interesting studies on the relation of nuclein to leucocytosis.

The observations were made on subjects in good general health, who presented no anomalies of nutrition, the diet being uniform and carefully weighed. The author thinks that the normal range in the number of leucocytes is so marked that no significance is to be attached to differences of a few hundred. He was able to produce a distinct leucocytosis by administering daily four pastilles, each containing one-half gramme of nuclein.

He found that nuclein administration exerted no influence over uric-acid excretion.

In a second experiment with pure nuclein he sought to ascertain whether it would be as completely absorbed as Weintraud had shown to be the case with nuclein-bearing thymus substance, the secretion of phosphoric acid increasing appreciably under the action of the thymus. For this purpose the urine for twenty-four hours was estimated for total nitrogen by Kjeldahl's method, for uric acid by Hopkins's method, and for total phosphoric acid by titration with uranium solution. The nitrogen content of the food, which was mixed, was estimated as accurately as possible by repeated analyses. The patient was 28 years of age. The result is shown in the following table:

Date.	Phosphoric acid.	No of leucocytes per cubic millimeter.
Normal days:		
June 29-30, 1895.....	1.91	
June 30-July 1.....	2.67	June 30: 7400.
July 1-2.....	2.93	
Nuclein days:		
July 2-3.....	3.10	
July 3-4.....	3.31	July 3: 10,300
July 4-5.....	3.23	
Normal days:		
July 5-6.....	2.6	
July 6-7.....	3.2	
July 7-8.....	2.9	July 7: 7900.

The absorption of the nuclein is confirmed by the increase of the secretion of phosphoric acid on the nuclein days. The slight increase accords entirely with the small quantity of nuclein, for in this experiment too only two grammes of nuclein were administered daily.

Dr. Herbert Maxon King, of Grand Rapids, Mich., publishes in the *Medical News* of May 22, 1897, a report of six experiments which he made upon tuberculous patients to

determine the effect of nuclein upon the blood, with special reference to the increase of polynuclear cells. In every instance the figures given state the contents of one cubic millimeter of blood, being an average derived from the contents of 256 cubic millimeters. Particular attention was paid to the digestive organs, in order to ensure the same conditions at the time of both examinations. The second examination in each case was made in from three to five hours after injection of 50 minims of a 5-per-cent. solution of nucleic acid [as manufactured by Parke, Davis & Co.]. In Experiment IV the temperature was 98.4° at the time of each examination; in Experiment VI it was 102.6° at the time of the first examination and 101.1° at the time of the second; in all the other cases the temperature was slightly above normal at the time of the first examination, and from one-tenth of a degree to one and seven-tenths degrees higher after the injection. The pulse varied from 68 to 120.

	Before injection.	After injection
EXPERIMENT I:		
No. of leucocytes.....	10,900	15,900
Mononuclear cells.....	5,900	5,600
Polynuclear cells.....	5,000	10,300
EXPERIMENT II:		
No. of leucocytes.....	13,100	18,100
Mononuclear cells.....	6,250	5,950
Polynuclear cells.....	6,850	12,150
EXPERIMENT III:		
No. of leucocytes	9,050	17,800
Mononuclear cells.....	3,750	6,550
Polynuclear cells.....	5,300	11,250
EXPERIMENT IV:		
No. of leucocytes	10,300	11,550
Mononuclear cells.....	5,650	4,400
Polynuclear cells	4,650	7,150
EXPERIMENT V:		
No. of leucocytes.....	9,050	11,850
Mononuclear cells.....	6,550	3,100
Polynuclear cells.....	2,500	8,750

	Before injection.	After injection.
EXPERIMENT VI:		
No. of leucocytes.....	17,150	19,050
Mononuclear cells.....	5,300	10,000
Polynuclear cells.....	11,850	9,050

Two control experiments upon healthy adults yielded the following results:

	Before injection.	After injection.
EXPERIMENT I:		
No. of leucocytes.....	6,250	33,400
Mononuclear cells.....	2,500	12,800
Polynuclear cells.....	3,750	20,600
EXPERIMENT II:		
No. of leucocytes.....	5,300	21,850
Mononuclear cells	2,800	6,550
Polynuclear cells.....	2,500	15,300

Dr. N. S. Davis, Jr., of Chicago, in the course of a paper on "The Treatment of Consumption," published in *Medicine* for August, 1896, states:

Nuclein possesses antiseptic properties, but above all the power of provoking a vigorous leucocytosis, which, it may be hoped, will stimulate the tissues to a more successful resistance of invading micro-organisms. It has been claimed for nuclein that it is of use in tuberculosis and suppurative disorders. In the latter class of cases it has often seemed to me useful, but in cases of mixed infection—*infection by the bacillus tuberculosis* and by pyogenic organisms—it has not done good. When suppuration is threatening from invasion of a tissue by streptococci or staphylococci, I have many times observed apparent inhibition of the suppurative process by means of nuclein treatment. This success tempts me to continue experimenting with the drug, even in tuberculosis. I have witnessed no ill-effects from its employment; no effects upon bodily temperature, circulation, excretion of waste products, or general nutrition, except such as might be induced by favorable changes in the inflamed tissues.

The Nature of the Leucocytosis Produced by Nuclein Acid.

Delano Ames, A.B., M.D., and A. A. Huntley, M.D., of the Baltimore Medical College, report the results of their preliminary experiments on this subject to the *Journal of the American Medical Association*, Sept. 4, 1897. Following is an abstract of their contribution:

Since the germicidal property of normal blood resides in a substance known as nuclein, and since this is derived from the nuclei of certain cells of the blood, the white corpuscles, it is believed that by increasing the number of these cells very materially the germicidal power of the blood plasma may be considerably heightened.

One of the constant results of the injection of nuclein, or of its administration per os, is the production of an apparent leucocytosis, meaning by that term an actual increase in the total number of leucocytes per cubic millimeter, circulating in the blood. The word "apparent" is here used advisedly because it is claimed by some writers that the increase is only apparent, not real. It can readily be seen that on the determination of this important point the value of this or of any similar preparation will rest. If the results following the administration of nuclein consist only of a rearrangement of the leucocytes in the different portions of the circulation, and not of an actual increase in the number of the same, we cannot hope by its use to augment the germicidal power of the blood, since we cannot increase those bodies, the white corpuscles, that produce the germicidal substance.

The arguments advanced in support of the view that leucocytosis is but an affair of distribution are worthy of very careful examination. There are two chief ones on which the theory rests. In the first place it is claimed that the apparent increase in the number of cells occurs chiefly in the polymorphonuclear variety which, if we accept Uskow's theory and classification, are the mature elements. If it is true that an actual new formation of cells takes place as the result of the injection of nuclein, the claim is made that we should find the greatest

percentage increase in the mononuclear or young elements. In the second place it is claimed that an examination of the blood shows that while there is an apparent increase in the number of cells in the peripheral vessels the central circulation shows a corresponding paucity of cellular elements.

The experiments we made were all upon medium-sized dogs, and while we will not detail each one we will give the steps pursued and a few of the results which are typical of all, since with very slight variations practically the same results were obtained in all cases. Before putting the dog under ether a count was made of the leucocytes in the peripheral circulation. Ether was then administered and the same was done for the peripheral and central circulations. We made the count of the peripheral circulation before the administration of ether, because we found that the ether alone produced some increase in the number of leucocytes, the amount seeming to depend on the rapidity or slowness with which the animal succumbed to the anesthetic; a greater change was noted in those dogs that struggled the most and required the most ether. After making the counts already mentioned, a hypodermic injection of nuclein solution (1 per cent., P. D. & Co.), varying from 25 to 45 minims in the different experiments, was given, and counts made from both the peripheral and central circulations every five minutes thereafter, up to thirty-five minutes in some cases. Care was taken to allow the animal to bleed but little, and as slight disturbance was produced by the operation as possible.

The leucocytes in the blood withdrawn were stained with a weak solution of methyl violet in normal salt solution, and the results of the various counts tabulated. In every instance ten counts at least were made and the average taken. The entire field of the blood-counter was counted every time. In this way it was hoped to reduce the limit of error as much as possible. The general results of these experiments may be summed up as follows:

1. The administration of ether alone causes an increase in the number of leucocytes over that found in the circulation before its administration. The amount of the increase seems

to depend on the amount of ether used and the time required to anesthetize the animal.

2. Before the administration of nuclein the counts showed that the number of leucocytes in the peripheral and in the central circulation was practically the same, varying only within the limit of error, or slightly over, sometimes one way sometimes the other.

3. Following the administration of nuclein solution there was immediately, that is by the end of five or ten minutes, a noticeable increase in the number of leucocytes *in both the central and peripheral circulation.*

4. At this time the percentage increase was most marked in the young mononuclear forms, which in some instances rose as high as 60 per cent. of the whole within fifteen minutes, while at the same time the proportion of polymorphonuclear elements was proportionately low.

5. The longer after the injection of nuclein the greater was the actual increase, and the number seemed to steadily rise *in both the peripheral and central circulation.*

Nuclein in Tuberculosis.

The most elaborate report so far published on the use of nuclein in tuberculosis is that of Prof. Victor C. Vaughan, which appeared serially in the *Medical News*, running from February 27 to March 27, 1897. A portion of this exhaustive paper is a *résumé* of lecture material presented by the author in his capacity as Professor of Hygiene and Physiological Chemistry in the University of Michigan, and makes highly interesting reading, discussing as it does the pathology and curability of tuberculous processes in general. Following this discussion is a report of the author's clinical experience with nuclein in the treatment of tuberculosis, including a review of 24 cases reported in 1894, and aggregating in all 76 cases, 70 of which were pulmonary. We reproduce Dr. Vaughan's summary and conclusions:

Summary.—The cases reported in this and the preceding include all those in which the tubercle bacillus was

found, treated by me with yeast nucleinic acid, from May, 1893, to December, 1895. There has been no selection of cases to report, and no exclusion. Many were in the last stages of the disease when the treatment was begun. Indeed, some of them were at that time confined to their rooms, and died within a few weeks. In my study of the value of yeast nucleinic acid in the treatment of tuberculosis, I have endeavored to carry out the investigation as I would a series of laboratory experiments, and, above all, not to deceive myself. Of the seventy-six cases reported, seventy are those of pulmonary tuberculosis. Of these, thirty (42 $\frac{1}{2}$ per cent.) have died. Of these, at least nine were temporarily benefited.

Of the seventy, seventeen (24 $\frac{1}{2}$ per cent.) have been continuously free from the bacillus for from one month to two and one-half years, so far as can be determined from the sputum; *i.e.*, either there has been during this time no sputum to examine or that examined has failed to reveal the bacillus. To the best of my knowledge, another (No. 47) has been free from the bacillus for more than a year, and another (No. 29) has been free from the bacillus with the exception of a short time, and still another (No. 24) was free when last examined. Twenty (28 $\frac{1}{2}$ per cent.) were still infected at the last examination. Of these, sixteen have been apparently improved by the treatment. It should be stated that none of these were hospital cases. I was not able to control their diet. Most of them were not rich, and had only inexpensive food. The hygienic conditions under which many of them have lived have not been satisfactory.

Of the five cases of urinary tuberculosis, four have apparently been cured. One was temporarily benefited, but developed acute miliary tuberculosis and died. The one case of joint tuberculosis has been benefited.

Conclusions.—I have reached certain positive and definite conclusions concerning the value of the one-per-cent. solution of yeast nucleinic acid in tuberculosis, administered daily in doses of from 60 to 80 minimis hypodermically, and these conclusions I will now give:

1. In advanced stages of the disease, in which the area of involvement is great, with or without cavities, the best that can be expected from this treatment is temporary improvement. Even this does not occur in all cases.

2. In initial cases, when the area of infection is limited, this treatment may, and often does, not only arrest the progress of the disease, but it acts as a curative agent.

If these conclusions be correct, it follows that in order to save our tuberculous patients by the employment of this treatment we must recognize the disease in its incipiency.

I will put in condensed form my ideas concerning the means which should be employed in the early recognition of tuberculosis:

1. Whenever there is any sputum it should be examined for tubercle bacilli. If the bacilli are not found in the first examination the search for them is to be repeated. When the bacilli are present the diagnosis of tuberculosis is positive. Failure to find bacilli, even after repeated examinations, does not prove the absence of tuberculosis. The complete absence of cough and of sputum is not proof of the non-existence of tuberculosis.

2. Apical catarrh, even when no bacilli are found in the sputum, is in the great majority of instances due to tuberculosis. Leube is certainly right when he says: "Marked dullness of the percussion note over the apex is always ('fast immer') a symptom of pulmonary tuberculosis, especially when the dullness is unilateral, and is detectable also in the infraclavicular fossa or in the regio supraspinata. . . . Still more certain is the diagnosis when the dullness on percussion is accompanied by auscultatory variations from the normal. The slightest variations in the respiratory sounds suffice here, such as jerky breathing, prolonged expiration, feeble or intensified, or rough vesicular breathing, and indefinite respiratory sounds. If the breathing be of bronchial character, or if there be râles, even when these are isolated, the slightest percussion dullness in the apex becomes of great diagnostic significance."

Among the very earliest variations in respiratory sounds in

tuberculosis is a prolonged expiratory movement. When this is accompanied by retraction of the apex and dullness on percussion, there can be but little doubt about the diagnosis.

In the *Medical News* of May 22, 1897, Dr. Herbert Maxon King, of Grand Rapids, Mich., narrates his experience with yeast nuclein in the treatment of tuberculosis. He has employed various strengths, as these have been offered through improvements in manufacture. He selects, as a rule the subcutaneous areolar tissue overlying the gluteal muscles, as the point for injection, avoiding in particular the arms, legs and thighs on account of the pain and local reaction induced by injection in these localities. Thrusting the needle in to its full length (one inch) at an angle of about 75 degrees, he injects slowly, 50 minimis requiring a quarter of a minute's time.

In the 37 cases summarized by the author from his own practice, microscopical examination confirmed the diagnosis of tuberculosis in all but three; and in these three the evidences were such as to leave no doubt of the tuberculous character of the lesions. The average age of the patients was 31.2 years, the extremes being 16 and 61 respectively. Eighteen were complicated by tuberculous disease elsewhere than in the lungs. The author divides his cases into four classes, as follows:

	No	Stage.			Complications.		
		Incipient.	Advanced.	Far advanced.	Uncomplicated.	Laryngeal complications.	Other complications.
I. Patients treated 1 month or less	10	2			5		
II. Patients treated 1 to 3 mos.....	12	2	4	3	7	3	2
III. Patients treated 3 to 12 mos.....	12	1	2	3	4	3	0
IV. Patients treated more than 1 yr.	3				0	0	0

The results obtained were:

	No.	Apparently cured.	Disease arrested.	Improved.	Unimproved.	Died during treatment.	Died after cessation of treatment.	Present condition unknown.	Known to be living.
I. Of the cases treated 1 month or less.....	10	1	0	0	9	0	5	1	4
II. Of the cases treated 1 to 3 months.....	12	3	2	4	3	1	0	3	8
III. Of the cases treated 3 to 12 months.....	12	3	3	2	4	2	3	0	7
IV. Of the cases treated more than 1 year	3	1	2	0	0	0	0	2	3

GENERAL RESULTS.

Apparently cured.....	8
Disease arrested.....	7
Improved.....	6
Unimproved.....	16
Died during treatment.....	3
Died after cessation of treatment.....	8
Present condition unknown	6
Known to be living.....	22

A great majority of the patients were members of families of very limited means, unable to procure any of the luxuries and deprived of many of the necessities of invalid life. So far as possible, hygienic conditions were improved, and strict attention was given to the general supportive treatment and nutrition.

Of the 34 patients whose sputa contained tubercle bacilli, only eight exhibited this diagnostic sign after the treatment with nuclein. Sixteen of the cases gained in weight, and 11 lost weight, under the treatment.

Dr. King concludes that nuclein, while not a specific in tuberculosis, is a perfectly logical remedy which acts in unison with, and as a stimulant to, the physiologic function of animal resistance to the invasion of disease; and that it has given far better clinical results in tuberculosis (by actual statistics) than any other medicinal agent heretofore employed in the treatment of this disease.

S. H. Wellings, M.D., of Detroit, Mich., writes in the *Medical Age* of July 25, 1899, as follows:

It is evident from current medical literature, and from results of the recent meeting of the Tuberculosis Congress held in Berlin, that no specific cure for tuberculosis has been found. It appears certain that the profession will still have to be prepared to meet with many discouraging failures in the treatment of this dread disease with the remedies now at hand, until some specific is found. The labors of the profession have not been entirely barren of results, however, for many useful lessons have been learned concerning the management of consumptives, and several new and promising remedies, each having more or less reputation for utility, have recently been brought forward.

Conspicuous among new remedies recently recommended by well known authors is nuclein solution. It is not my intention to discuss the comparative merits of the many new remedies enjoying more or less notoriety, but simply to give my personal experience in the treatment of four cases of tuberculosis with nuclein solution.

Case 1.—A girl aged seventeen, whose father died of pulmonary tuberculosis about two months previous to her first visit to my office. He was confined to his home for several weeks, and cared for by the family during his last illness. This girl was robust and healthy looking and appeared to be free from any disease up to within two or three weeks prior to her father's death. The mother and three sisters are all healthy. At the time of her first visit the patient was coughing and raising sputum freely, and her weight was 98 pounds. The temperature ranged from 101° to 102°; night-sweats were profuse and exhausting. Menstruation had ceased and was never again restored, while emaciation was extreme and progressed rapidly. The girl was troubled with distressing nausea and loss of appetite. Dullness was noted over the upper half of the right lung, and moist râles were heard over the balance of the pulmonary surface. Diarrhea and frequent paroxysms of abdominal pain complicated the condition. The microscope revealed an abundance of tubercle bacilli in the sputum. The

prognosis was not promising in this case, and I so informed the mother. I commenced treatment May 5, 1897, by injecting in the arm ten minims of a five-per-cent. nuclein solution. I gave an opiate to control the pain, and directed the patient to take as much exercise in the open air as possible. May 7, the temperature being 102° , I injected fifteen minims in the arm. On May 8 twenty minims was given; the opium was discontinued, it being no longer needed. May 10 I noticed a slight improvement, signalized by a drop in the temperature, the thermometer registering 101° . On May 12 my patient complained of having experienced a slight reaction after the last injection, and stated that she did not feel able to come to the office on the 11th. After the subsequent injections I usually noticed a trifling febrile reaction of transient duration. From May 12 until June 28, inclusive, this patient was given an injection every other day; I increased the dose each time till it reached 60 minims, and then continued without further increase. The period from May 12 to June 1 witnessed an improvement in her general condition, the temperature dropping at one time as low as 100° . After June 1 she grew rapidly worse, until death finally ended her sufferings, July 15, 1897. I always sterilized with carbolic solution previous to inserting the needle, protected the puncture after each injection with iodoform collodion, and in no instance was there an abscess or any local trouble other than a slight transitory induration and redness.

Case 2.—This was a man twenty-three years of age, single, a common laborer, whose father and mother were living. One sister and an uncle died of pulmonary tuberculosis. This man took cold one year previous and was never well afterward. I first saw him at his home, where I found him in bed. His temperature was ranging from 102° to 103° ; he had night sweats, with profuse and exhausting expectoration. He could take but little food owing to irritability of the stomach; he was unable to leave his bed, could not sleep well in consequence of excessive coughing, and was extremely emaciated. I discovered that there had been an extensive loss of lung tissue on the right side. I shall omit detailed description of the daily

treatment in this case. It seemed a hopeless undertaking from the beginning. The patient would not consent to the use of injections of nuclein solution. I therefore directed him to take it by the mouth, in teaspoonful doses, three times a day. He began to improve from the commencement of the treatment. In about two weeks he was able to walk about the yard and could take more food. He continued to improve for about six weeks, when he began to fail, and died in about five months from the time of beginning the treatment.

Case 3.—F. O.—, a boy aged sixteen, a student, whose father and mother are living but in poor health. The father has chronic naso-pharyngeal catarrh. There were no other children in the family. An aunt on the father's side died of pulmonary tuberculosis. The boy was sent to me from his home, about 125 miles distant. At that time he complained of pain in the right side, over the lower lobe of the right lung. He was nauseated frequently, and occasionally vomited after taking food. He coughed almost constantly, and raised thick yellow sputum. His weight was 97 pounds. The temperature registered 101° to 102°. On percussion I observed dullness over the lower lobe of the right lung. Auscultation revealed the presence of moist râles. The patient experienced dyspnea on taking exercise. He could sit up, but was able to take but little exercise without causing great fatigue. A bacteriological examination of the sputum revealed tubercle bacilli. I immediately began to use nuclein solution injections of twenty minims once daily, increasing the dose each day by easy stages. I had to abandon the injections after about two weeks, since the boy was so nervous and the injections caused so much excitement. I concluded it more prudent to adopt the oral method of medication, which resulted in a decided improvement from the beginning. He began to gain in weight, his temperature gradually diminished, and in three weeks his condition was so encouraging that I sent him home with a supply of nuclein solution five-per-cent., and gave him instructions to take one teaspoonful three times daily. He sent me daily written reports, which testified to his steady and uninterrupted recovery. In three months his temperature continued

nearly normal, and his weight had reached 120 pounds. He could easily walk ten or fifteen miles a day. It is now two years since I saw him, and the young man is pursuing his studies in college. He informs me his health is good and he has no trouble whatever. He continued the medicine about seven months.

Case 4.—Miss G. W.—, aged twenty years, by occupation a saleslady in a dry goods store. Her mother is living and healthy, but her father died of some chronic lung trouble, probably tuberculosis. The patient's weight was 98 pounds, her temperature 102°, she had night sweats, and the catamenia had been suppressed for four months. She had a poor appetite, suffered with constipation, and complained of being tired all the time. On physical examination I found dullness over the apex of the right lung, but no cavities. Tubercle bacilli were profusely distributed throughout the sputum; the cough was distressing, often disturbing the sleep at night. The sputum was copious and streaked with blood; usually it was thick and purulent. Treatment began April 18, 1898, by taking teaspoonful doses of nuclein solution No. 2 (for oral use only) three times daily. This treatment was followed faithfully for about four months, interrupted only by a few short intervals during which the medicine had to be omitted owing to its disturbing the stomach. Soon after beginning the treatment a general improvement was noticed. This patient is now occupied in her usual avocation; she eats well, has no cough, her menses have been restored, and she appears well. No examination for bacilli in this or the previous case since recovery.

The nuclein solution used in all these cases was the five-per-cent. solution prepared by Parke, Davis & Co., of Detroit. In the first three cases the solution for hypodermic use was employed, and in Case 4 the No. 2 solution, five-per-cent., was taken by the mouth only.

Following is an abstract of a paper contributed by Dr. M. O. Teigen, of Minneapolis, Minn., to the *Therapeutic Gazette for June, 1895*:

Since November last, four cases of pulmonary tuberculosis, of not very long standing, have come under the writer's care, three of whom, up till the 1st of February, had been taking for phthisis creosote, cod-liver oil, arsenic, hydriodic acid, terebene, and a carefully selected diet, aided by digestants. They all made some improvement under that treatment up to a certain limit, beyond which they evidently could not pass. I then advised them to give Professor Vaughan's nuclein a trial. The results are stated below:

Case 1.—P. P.—, aged 19, farmer, was examined by me on the 16th of December last. Two sisters had died of phthisis pulmonalis at about his age. He was very pale, anemic, emaciated, and weak, and had been so for a month and a half. Appetite and digestion very poor. A harassing cough kept him constantly awake, and night-sweats and hectic fever were present every night. Evening temperature usually about 101°; pulse about 120. Chest expansion amounted to less than two inches; dullness over right apex; high-pitched breathing. Tubercle bacilli numerous.

The ordinary methods of treating phthisis resulted in some improvement, but it was not until he began to receive nuclein (Parke, Davis & Co.), on February 28th, that he began to markedly improve. He received 15 drops hypodermically every day for five weeks, and during this time gained fifteen pounds. The cough and expectoration decreased, as also the number of tubercle bacilli. He eats like a harvest-hand, and insists he is growing "tougher" day by day so far as endurance is concerned. With pulse and temperature normal, and the evidences of apical induration gradually receding, he now presents the appearance of a fairly healthy youth.

Case 2.—Miss A. P.—, aged 19, a domestic, had been ailing for eight months. I found her a tall, spare, narrow-chested, cachectic-looking woman, with a tubercular appearance. An elderly sister had died of phthisis florida. The weight of the patient was 109 pounds. Evening fever and night sweats, usually. Throat sore, but appetite and digestion fair. Menstruation had been absent since March, 1894.

(ten months). Cough was very persistent, often keeping her awake at night; sputa yellowish gray and viscid. Temperature 100°; pulse 95 and unsteady; respiration 28 to 30, and diminished over right apex. Dullness and increased vocal fremitus very marked over affected areas. In brief, a typical case of incipient pulmonary tuberculosis was before me.

The treatment consisted in the use of creosote by the mouth and its vaporization in the room of the patient, and in the internal administration of cod-liver oil and terebene. Under this she gained 6½ pounds and expressed herself as much improved. Nuclein (P., D. & Co.) was now given in gradually increasing doses, with still greater evidences of improvement. The night sweats became less and the febrile movement decreased. The average gain in weight for several weeks now amounts to 2½ pounds a week, and she is elated over her ability to take long walks. Menstruation has been re-established, and, notwithstanding a recent mild attack of influenza, her recovery does not seem to be retarded.

Added to the other encouraging indications of improvement comes a plainly discernible decrease of vocal fremitus and percussion dullness over the affected area, and increased expansion and respiration. Electricity cataphoretically has likewise been employed in her case with seeming benefit.

Case 3.—O. B.—, a North Dakota farm laborer (previously a bar-tender), contracted a severe laryngo-tracheitis and bronchitis. He lost 25 pounds in three months; weighed 117 pounds when examined on the 5th of March last. Pulse 122; temperature 99½; appetite nil; vomiting, sore throat, hoarseness, persistent cough, copious muco-purulent expectoration, regular night-sweats after evening fever. Laryngoscopic examination revealed ulceration and tumefaction of epiglottis and vocal cord. Laryngeal exudate contained an abundance of tubercle bacilli. A small area in lower part of left upper lobe presented decreased respiratory murmur, perceptible dullness, and high-pitched percussion sound. Diagnosis, laryngeal and pulmonary tuberculosis.

Was at once put upon nuclein (P., D. & Co.) hypodermically and by atomizer, hematics, and digestants. The first

ten days of treatment he gained two pounds in weight, and expressed himself as stronger from day to day. The night-sweats decreased, and eventually ceased altogether.

From the tenth day he grew steadily weaker and worse; cough, expectoration and dyspnea increased, the night-sweats returned, and, it becoming apparent that the end could not be far off, he was sent back home, with no ultimate benefit accruing from the nuclein treatment.

Case 4.—Mrs. H. S——, age 33, farmer's wife, was suddenly taken three years ago in June with severe paroxysmal cough and dyspnea; the cough continued with but little amelioration up till examination in October last. Emphysema of the lungs, bronchiectasis, and incipient pulmonary tuberculosis of a slowly progressive character, were diagnosed. Creosote, cod-liver oil and hydriodic acid helped her somewhat, but the cough, expectoration, hectic and night-sweats continued. Nucléin (P., D. & Co.) was given secundum artem, conjoined with electricity, and this treatment arrested the profuse night-sweats after five days' exhibition. She took the treatment about two weeks, but, becoming discouraged with the slow progress made, unexpectedly started for home, and all traces of her case were lost to me.

Frank W. Garber, B.S., M.D., of Muskegon, Mich., in January, 1895, reported through the columns of the *Therapeutic Gazette* several cases of apparent tuberculosis—bacteriological verification lacking—which manifested marked improvement under nuclein.

In the first case a month's treatment with nuclein reduced the temperature from 100°-102° to normal, improved the appetite, reduced the cough, and abolished the night-sweats. In six weeks the patient, a married woman of 39, had gained 12 pounds in weight; and menstruation, which had been suspended for several months, was re-established.

Following six months of the usual treatment, without improvement, nuclein was given on alternate days in the case of Mrs. B——, aged 28, who was suffering from anorexia, hectic,

night-sweats, emaciation, etc. In six weeks the cough had decreased, night-sweats disappeared, appetite improved, fever declined, and patient had gained three pounds in weight.

A gentleman of 40 years, who exhibited percussion dullness over both apices, together with laryngitis, a harassing cough, and all the ordinary signs of advanced phthisis pulmonalis, gained seven pounds in four weeks under nuclein, 30 minims daily. Improvement was manifest in the cough, the throat symptoms, and the appetite.

A young cigarmaker who presented a large glandular swelling, extending from the angle of the left jaw down to the clavicle, with emaciation, anemia, hectic, night-sweats, and anorexia, showed marked general improvement under treatment with nuclein, which was injected directly into the swelling, diagnosed tubercular lymphadenitis; this swelling diminished one-half in size.

A grocer aged 30, who had experienced a pulmonary hemorrhage in June, 1894, was examined in the following October, when almost the entire right lung was found to be involved; with constant cough, an evening temperature of 103°, night-sweats, anorexia, and emaciation, there seemed no escape from the diagnosis of tuberculosis. Under nuclein, in less than six weeks the patient had gained eight pounds, the night-sweats had almost entirely ceased, the temperature was normal, and the cough much improved; physical signs unchanged; patient feeling well.

A patient 32 years of age, with extensive infiltration of the right lung, grew rapidly worse notwithstanding nuclein treatment.

A housewife aged 65, with slight dullness over left apex, incessant cough, poor appetite, and much digestive disturbance, in whose case a diagnosis of incipient tuberculosis was made, gained three pounds under nuclein treatment, and became in all respects better.

Another patient, aged 28, who showed all the rational signs of tuberculosis, made a steady gain in every way under nuclein treatment.

In all of Dr. Garber's cases the preparation used was the

1-per-cent. solution then manufactured by Parke, Davis & Co.]

In the *Therapeutic Gazette* for August, 1895, Prof. R. W. Wilcox, of New York, reported a case of pulmonary tuberculosis materially benefited, if not cured, by nuclein injections. The patient was a young man of 24 years, who dated his illness from a cold contracted eight months previous to examination, and who had suffered several free hemorrhages from nose and mouth, generally preceded by coughing. The more striking symptoms when the case was first taken in hand were: dyspnea, cough, muco-purulent and bloody expectoration, fever, areas of percussion dullness, etc. Microscopical examination of sputum showed innumerable tubercle bacilli. Nuclein (Parke, Davis & Co.) was given hypodermatically, beginning with 10 minims twice daily and increasing by 5 minims a day until the dose reached 40 minims twice daily. In less than a month the bacilli had disappeared, apparently; microscopic investigation at this time and thrice afterwards, covering altogether a period of six weeks, failed to detect the germ. The patient had then—some two months and a half from the date of consultation—so far improved as to be at work, and no further report was made by him.

Dr. A. J. Rosenberry, of Wausau, Wis., writes in the *Therapeutic Gazette*, October, 1895, as follows:

If the theory of phagocytosis be true, the great object to be attained by the therapist is to furnish all the cells of the body with appropriate pabulum, and to increase the number of white cells. That we have in nuclein a substance which furnishes this cell food in a form in which it can be readily utilized, seems quite certain. That it increases the number of white blood-cells enormously has been demonstrated by the work of Vaughan, McClintock, and Warthin.

Having had experimental knowledge of the action of nuclein in my own case, I wish to record it, in the hope that

others with larger opportunities for testing its merits may be induced to give it a trial, for, living, as I do, in a belt that is practically non-tubercular, opportunities for testing it are not frequent.

On February 28, 1894, I passed a large quantity of blood and some pus with my urine. Upon boiling the urine, three-fourths by volume solidified, showing the presence of rather more albumin than the blood would account for. Two of my colleagues agreed upon the diagnosis of renal congestion. In accordance with this I was dry-cupped and purged for a week, when the urine became normal. Meanwhile a specimen had been sent to Dr. V. C. Vaughan, of Ann Arbor, and tubercle bacilli were detected.

I was then forty-two years of age, with no history of tuberculosis in any branch of the family. My health had always been good up to June, 1893. My weight at the time of illness (March, 1894) was 195 pounds, and I was surprised at the diagnosis of genito-urinary tuberculosis made by Dr. Vaughan. However, I at once proceeded to Ann Arbor to place myself in his hands for treatment. He proposed the nuclein treatment, of which I had not even heard at that time.

After a day's consideration I decided to accept his plan and give it a trial. On March 20, 1894, the first injection of $\frac{1}{2}$ drachm was given. The quantity was rapidly increased until the daily dose reached $1\frac{1}{2}$ drachms, when chills, fever, vomiting and general malaise supervened. The injections were discontinued until the unfavorable symptoms had disappeared, then resumed in smaller doses, about $\frac{1}{2}$ drachm being the highest dose I could bear. With the large doses there was also a quite severe local reaction at the point of injection. A swelling four inches in diameter and two inches in thickness formed, and remained hot and painful for several days, but disappeared without suppuration. No pus ever formed at site of injection. From April 1 to November 20, 1894, daily injections were taken. My general health steadily improved; the local symptoms, which at no time amounted to more than slight uneasiness and a dull, heavy

feeling at the neck of the bladder, disappeared; only one hemorrhage occurred. At present my general health is excellent.

Wishing "to make assurance doubly sure," I called, June 8, 1895, upon a surgeon of international reputation in Chicago for a digital examination. A cursory examination satisfied him that I had tuberculosis of the left epididymis too far advanced for operation. Guaiacol and change to a mild climate were advised.

Two weeks later I was given a most searching examination by that brilliant diagnostician, Dr. John B. Murphy, of Chicago, who was unable to find any evidence whatever of tuberculosis. He suggested that if the urine gave no evidence of tuberculosis of the kidney, the disease had been eradicated—cured. Acting on this suggestion, the urine was at once thoroughly examined at the University of Michigan Hospital, at Ann Arbor, with negative results. I therefore regard myself as having made a complete recovery.

The chemistry of the nucleins has not, I believe, been accurately determined. Foster's "Physiology" gives an approximate formula. It is agreed by all that nuclein contains a high percentage of phosphorus in a non-toxic form. The first sample used was that manufactured in the laboratory of the Michigan University; later I used that made by Parke, Davis & Co., after the same formula.

When properly prepared and kept in glass-stoppered bottles, nuclein will keep indefinitely. When kept in cork-stoppered bottles decomposition occurs, with the formation of toxins, which, when introduced into the circulation, produce the same symptoms produced by overdoses—viz., chills, fever, nausea, and vomiting.

I have used it myself in two cases of pulmonary tuberculosis. The first case was far advanced, a cavity having formed, there being hectic, night-sweats, emaciation, etc. No effect was produced.

In the second case the patient was treated for three weeks only. Two months later a cavity formed and a hemorrhage occurred. A trip to Florida was followed by great improve-

ment. At last accounts the patient was living at Manitou, Col., and was free from tuberculosis.

I believe that in nuclein we have a remedy of great value, especially in the incipient stages of the disease. Its absolute innocuousness, its abundance and consequent cheapness, and its tonic properties, are in sharp contrast to the toxic destructive action of some of the recently advocated remedies for this disease.

Dr. R. L. Botsford, of Moncton, N. B., reports the following case in the *Medical Age* of Nov. 10, 1897:

William S—, about 38 years of age, a well-to-do farmer, suffered with tuberculosis of the bladder for eighteen months. The disease was not correctly diagnosed until he paid a visit to the Victoria General Hospital in Montreal, when the case was pronounced incurable, and he returned home to die.

I was consulted by friends of the patient, and told them I had heard of nuclein solution through literature furnished by Parke, Davis & Co., and advised its use. It was employed, really as a last resort. At this time he was suffering excruciating pain in the bladder and rectum, the pain running through the lower extremities, with desire to pass urine every fifteen minutes day and night; he also passed shreds of the lining of the bowels per rectum. The bearing-down pains were so severe that he had to place one foot on a chair and lean forward; in this position he felt more ease. His appearance was like a man of 80, and he stooped and had to support himself with a cane. The urine had been examined microscopically and found to contain the bacilli of tuberculosis.

Treatment was commenced on March 5th, 1894, with daily hypodermatic injections of nuclein solution, 1-per-cent. (P., D. & Co.), in the muscular part of the thigh, commencing with ten minimis and increasing daily until eighty minimis was reached, which was continued until May 15th, when he commenced taking the 5-per-cent. solution by the mouth. His urine was examined frequently and found gradually to

contain fewer and fewer bacilli, until ultimately, after a searching examination, it was found to be completely free.

Three weeks after the treatment began improvement was very noticeable, the pains gradually decreasing and becoming bearable; and instead of passing urine every fifteen minutes he was able to go without micturition from two to three hours. He soon began to take daily exercise and improved rapidly.

In September he was out on the farm working in the fields.

Dr. J. H. Hindman, of Admire, Kansas, reports the following case:

Mr. D—, aged 31, Scotchman, applied to me for treatment December 17, 1895. Tuberculosis of apex of left lung, of nine months' standing; two hemorrhages. All the rational signs of the disease were present—emaciation, hectic spots, loss of appetite, night-sweats, lack of strength on the least exertion. Evening temperature, 102.5°. Patient had been under ordinary treatment by physicians in Scotland, and as a last resort they ordered him to go to America.

On December 18, 1895, I placed him on nuclein treatment (Parke, Davis & Co.'s solution), which he took daily until March 18, 1896. His cough ceased, night-sweats disappeared, temperature fell to 99°, appetite increased, general appearance improved greatly, and he has gained nine pounds in weight. Patient is now doing light work on a farm.—*Therapeutic Notes*, October, 1896.

A lady of a tuberculous family history has complained of ill-health since February, 1895. I saw her early in March, when I found an area of dullness in the apex of the right lung, cough, expectoration, wasting, night-sweats, temperature in the evening averaging 100.5°, pulse 100 to 110, loss of appetite and flesh, and all the symptoms of tuberculosis. Began to treat her with nuclein, and during March, April, May and June gave nothing else. Began with ten minims,

increasing three minims per day until the dose reached eighty minims.

The first change that occurred was a fall of temperature, followed by general symptoms of improvement, increased appetite, etc.; the area of dullness in right apex gradually cleared so that by July 1st it was impossible to detect anything wrong with the lung. She left me about this time, but is now visiting friends and writes she is "all right." I think a cure was effected. The injections were intra-muscular (pectoral muscles and muscles of the back), and there were no abscesses, though after one injection there was a slight redness that lasted until morning. Her pulse for a long time before she went away ranged from 60 to 64; appetite fair; slept well; able to take exercise without any shortness of breath.

In another case, aged nineteen, the apex of the right lung was slightly consolidated; breathing broncho-vesicular; temperature 99.5° in the evening; cough, expectoration; some râles over that portion of the lung,—considerable cough and expectoration in the morning. Put upon nuclein, ten minims at first, doses rapidly increased up to ninety minims (hypodermically). In two weeks he had gained two pounds; cough and expectoration were less, particularly in the early morning; physical signs unchanged. Examination of sputa showed tubercle bacilli.—N. F. CUNNINGHAM, M.D., Dartmouth, Nova Scotia, in *Medical Age*, April 25, 1896.

In Acute Pneumonia.

Saturday, Oct. 20, 1894, called to see Mr. B—, who was suffering from pneumonia of the lower lobe of the left lung, in the first stage; pulse 110; temperature 104° .

On the Wednesday following, the upper lobe became involved; about the same time the right lung was attacked with *bronchitis*; temperature 105° ; pulse 120; respiration 30. The *succeeding Friday* the patient was delirious and evidently in a dangerous condition; the cough was almost constant;

expectoration frothy and viscid, *not rusty*; consolidation of left lung complete; pulse feeble and 120; temperature 105°. I now regarded the case as hopeless. The left lung had been consolidated eight days, and the right had become involved, in the larger bronchi at least, and there were no apparent signs of resolution.

At my request, Messrs. Parke, Davis & Company placed at my service a liberal supply of *Nuclein*, and I commenced its use the following day (Saturday) by a dose of fifteen minims subcutaneously at 9 A.M., and repeated at 5.30 P.M.

Sunday morning there was a marked improvement in the bronchitis (of the right lung); expectoration less viscid and more profuse. Gave one drachm nuclein hypodermatically morning and evening. Evening temperature normal; pulse 100; mind clear. No marked change in left lung.

Monday I found the patient sitting up, and he remarked: "I have no more use for you." On examination I found the respiratory movements had returned sufficiently strong to be readily noticed; the bronchitis of the right lung had disappeared, and the left was clearing. Tuesday the patient was up, sitting by the stove; pulse 80; temperature normal. Wednesday I gave the last dose of nuclein. Thursday, patient dressed and walking about. Saturday I pronounced him well, and discontinued my visits.

It is interesting to note the nuclein was commenced at a time when there was the most danger—temperature 105°, pulse 130, and delirium. The improvement was simultaneous with the use of the medicament!

The researches of Metschnikoff, Kossel and others prove that the polynuclear white corpuscles are the defenders of the system against the invasion of disease germs; and their action seems to be explained by the fact set forth by Doctors Vaughan and McClintock, that the germicidal substance in the blood is the nuclein found in the white corpuscles. With these facts clearly established we can understand how the consolidated lung so quickly cleared up.—WM. C. STEVENS, M.D., Hospital Interne, College of Medicine and Surgery, Detroit, in *Therapeutic Notes*, October, 1895.

In Pleuritic Effusion.

C. W. F., aged 35, had pleuritic effusion of the lungs about five or six years ago, and was aspirated therefor; has since been under treatment by several physicians, and under advice has twice visited California, but with no benefit except rest from business cares. Has had two hemorrhages every year, a bad cough, and for the last year purulent expectoration and gradual wasting.

October 25 last, I began injecting ten minimis nuclein solution, increasing by five minimis per day until the daily dose reached fifty minimis—this is the most he has used. From October 25 to December 9 he gained two pounds in weight. There was no disturbance of either temperature or pulse, save on one occasion when the former rose one-tenth of a degree. His expectoration before treatment was copious and purulent, but now is very small in quantity and slightly frothy; cough very much moderated—in fact, his general health is better than it has been for years, and he is now able to go to his office regularly and give attention to his work. His friends remark upon his improved appearance and absence of cough, and he goes out in all weathers. Formerly he suffered considerably from shortness of breath with the slightest exertion, but now he takes exercise without this inconvenience. Does not object to the small amount of pain caused by injection, and no abscesses have formed since treatment began. Pulse never above 80, and no night-sweats either before or since treatment commenced.—C. J. MORSE, M.D., Amherst, Nova Scotia, in *Medical Age*, Jan. 25, 1896.

In Typhoid Fever.

Dr. A. M. Boyer, of Philadelphia, informs the editor of the *American Therapist* that he has aborted apparently typical typhoid fever by the administration of nuclein. At first he was inclined to believe the recoveries coincidences, but when ^{the class of cases that he had frequently seen develop} ^{in previous years got well one after another in a few}

days or a week, he could not gainsay the evidence though apparently incredible.

I was first tempted to try this agent in an apparently hopeless case of typhoid, after observing its striking benefits in other maladies. With the assistance of the interne of St. Mary's Hospital, in this city, I gave it a very thorough trial; reserving its use, however, for the *more severe and virulent cases*. It was employed as an abortive in "first-week cases," the total series of which numbered sixty. There was not a single death among the sixty cases, and in forty-two of these nuclein was the chief remedy employed.

Even more striking were the results accruing to nuclein in pneumonia. During three months it was employed in ten out of fifteen cases, with but one death. In one case the right apex was involved, and the patient was out of hospital but a week when he returned again, this time with the left apex inflamed. He was again put upon nuclein, with the result that a favorable crisis occurred on the eighth day.

I have made a more complete and elaborated report of these cases of typhoid and pneumonia to the Secretary of the State Board of Health.—F. HARKIN, M.D., Marquette, Mich., in *Therapeutic Notes*, June, 1896.

In Septicemia.

Walter Courtney, M.D., of Brainerd, Minn., contributed a highly interesting paper to the *Medical News* of September 25, 1897, in the course of which he stated:

A year ago last winter I had the privilege of working in Dr. Vaughan's private laboratory at the University of Michigan, and while there observed his experiments with yeast nucleinic acid on rabbits and guinea-pigs which had been inoculated with the bacillus tuberculosis, bacillus tetani, and bacillus anthracis, each in different animals. The marked inhibitory, and frequently curative, effect of the nuclein *treatment of these various infections, well measured in all by careful controls*, made a deep impression upon my mind.

After resuming my regular duties it was not long before I was confronted with the task of treating a severe case of septicemia. In considering the treatment I should pursue, I remembered the striking effects I had observed from the use of yeast nucleinic acid, and determined to try it, in conjunction with other remedies, in the treatment of my patient.

Nuclein is said to be distinctly germicidal, for certain bacteria at least. Whether its germicidal properties, when introduced into the living body, are wholly due to the promotion of leucocytosis, and consequent phagocytosis, or not, I am at this time unable to say. One thing seems to be certain, and that is that nuclein has no antitoxic properties. This has been demonstrated by Vaughan and McClintock in their series of experiments on rabbits and guinea-pigs with yeast nucleinic acid and the toxins of diphtheria and tetanus.

[Here follows a minute description of ten cases of septicemia in which the author employed nuclein, all but one of which recovered.]

From the histories given there can be no question as to their severity and seriousness, and the imputation of simple surgical fever to any would not be consistent with their clinical manifestations. To say that some may have been cases of sapremia would simply be begging the question. But, in order to avoid argument with the pathologists, we may justly claim that sapremia may be fatally serious.

In Case 7, which resulted fatally, administration of the yeast nucleinic acid was not begun as early as it should have been. During the first two days after admission it was thought the symptoms were due to irritation from the painful contusion and laceration of the hand rather than to serious microbial infection. After this the disease seemed wholly irresistible. That I permitted the proper time to pass before resorting to the use of a remedy which, by this time, had gained a place in my confidence, is a matter of deep regret to me.

Among the striking results of the treatment in this list of cases I might mention, first, the promptness with which the

general health was restored after convalescence had begun, and, second, the readiness with which the injured tissues, which had furnished the infection atrium, healed, this being very noticeable in all except in Case 2. (In this case the general health improved very rapidly, but the tissues of the stump remained for a long time sodden and very indolent.) These results are in decided contrast to my previous experience in the treatment of septicemia—that is, before using the yeast nucleinic acid. Then convalescence in a great many of the patients who recovered was slow; the pulse would long remain rapid and weak, the skin sallow and dull, and the nervous system considerably shaken. The treatment of the local condition, too, where injury and infection occurred, would often tax one's patience and ingenuity to the utmost.

In regard to the auxiliary treatment of these cases, I presume there will not be wanting those who will ask if this alone would not have accomplished the results obtained. I must in honesty admit that it might possibly have done so. On the other hand, with equal candor I am compelled to say that no other form of treatment previously employed by me ever yielded, in anything like the same number of cases, such satisfactory results. It is true, of course, that the number of cases treated with yeast nucleinic acid is not convincingly large; still I am encouraged to persevere with it, and with a considerable feeling of confidence.

In my opinion the most valuable forms of auxiliary treatment are those which will effect free elimination by all of the emunctories that may be pressed into service, so as to rid the system of all the toxins possible. This is important because it not only acts on the direct source of danger (the toxins), but often obviates or mitigates another ever-present danger, viz., auto-intoxication. After this I would place the free but judicious use of stimulants, among the best of which are strychnine and whiskey. The proper administration of food will at all times receive attention at the hands of the careful clinician.

As regards the use of yeast nucleinic acid in septicemia, there are several points to which I wish to invite attention:

1. It should be given at the earliest possible moment that septic infection is suspected. One should not wait for the typical and classic symptoms as given by text books. My observations have taught me to believe that if one waits until rigors, icterus, diarrhea, delirium or apathy, profuse perspiration and a foul-smelling and discharging wound are added to an abnormal increase in temperature and pulse-rate and a restless alertness on the part of the patient, to convince him that it is septicemia that must be dealt with, instead of surgical fever or something else, he has been guilty of a serious waste of most valuable time.

2. The nuclein should always, in septicemia at least, be given hypodermically, if possible, in order to secure prompt action of the given dose. If the one-per-cent. solution is used, at least 30 to 40 minims, undiluted, may be given every three or four hours. If the five-per-cent. solution be used, from ten to fifteen minims may be given every three or four hours, but ought to be diluted with distilled or at least with sterile water. This is necessary to avoid the local reaction which is sometimes caused when this solution is given undiluted. In my experience, the five-per-cent. solution is preferable, for one reason at least: it is always stable.

If it be true, as Wells states (*Medical News*, Oct. 17, 1896), that leucocytosis is to be regarded as a local condition, then injection of the nuclein ought to be, in the early stage, as near to the place of primary infection as possible. I have invariably made the injections into the cellular tissue and muscles of the chest.

3. The injection region should be examined daily in order to determine if local reaction can have anything to do with the patient's increased temperature and pulse-rate. If it has, it is due to one of two things: either to insufficient dilution of the 5-per-cent. nuclein solution, or to imperfect preparation of the skin or syringe.

The following simple conclusion is the only one I shall offer at the present time: The results of my work with yeast nucleic acid in septicemia are sufficiently encouraging to justify a feeling of confidence and a continuance of its use.

In Puerperal Septicemia.

Stimulated by the experiments of Von Jacksch, who first employed leucotactic remedies, especially pilocarpine, in severe cases of pneumonia in which little or no leucocytosis was taking place, Dr. Hofbauer, in the clinic of Professor Schauta, attempted treatment on the same lines in grave puerperal diseases. For the sake of uniformity he exclusively employed nuclein, which had a prompt leucotactic action, exhibited scarcely any disagreeable by - properties, and under the influence of the pancreatic secretion gave off nucleinic acid, which acted as a bactericide. He remarked the following effects in the course of his observations:

1. The General Condition: The influence on this was very marked, and often surprising. Patients who previously lay in an apathetic, half-slumbering state, gave a clear, satisfactory answer as to their condition, and looked bright.
2. Local: The puerperal ulcers cast off their sloughs with remarkable rapidity, soon showed fresh granulating surfaces, and quickly healed over. The discharge from endometritis improved so that washing out could be dispensed with, and simple vaginal injections with disinfecting solutions were all that was required.
3. The Temperature: Contrary to the observations of other authors, he observed within twelve to twenty-four hours after the first dose a high rise in temperature. In one case the temperature rose to 41.6° (C.), and then fell to 37.8° . In the following days, in the cases that ended favorably, the curve was lower, or irregular exacerbation terminated a crisis.
4. The Bony System: In almost all cases, tenderness of certain bones came on, varying very much. In some there was only slight tenderness of the tibiae; in others it reached a degree only met with in advanced leukæmia. This tenderness lasted several days, at most a week, and then disappeared without leaving any trace.
5. The increase in the uric acid observed by Horbaczewsky and others always unmistakably appeared.

The observations embraced seven cases, and the author abstained from formulating any definite conclusions. So much, however, appeared to be clear: that for the accomplishment of any therapeutic result the administration of leucotactics must be begun as early as possible.—*Medical Press and Circular* (abstract from *Centralblatt für Gynäkologie*, 1896, No. 7).

Henry M. Joy, M.D., of Grand Rapids, in the *Therapeutic Gazette* (May, 1897), says:

The treatment of puerperal septicemia must of necessity be considered from two standpoints, namely, surgical and medical. The first has for its consideration the removal or limitation as far as possible of the source from which the toxic elements are supplied to the blood; and the second the aiding of Nature in her efforts to overcome the poisons already in the system.

A report of the following case in connection with the fulfilment of the second indication will, I think, be of interest:

On December 10, 1896, I was called to attend Mrs. C— in her second confinement. I found the patient in good physical condition. The child was lying in second position, vertex presenting. The case was conducted with the greatest possible antiseptic precautions, and labor was completed naturally in about six hours. The patient being out of the city, I did not see her again until the morning of the sixth day, when I was hurriedly summoned to attend her. I found that the previous night she had had a severe chill lasting about an hour. At the time of my visit the temperature was 105°; pulse 150, feeble and thready; abdomen greatly distended and very tender on pressure; skin icteric; and a condition of marked apathy denoting most profound sepsis. A vaginal douche of creolin solution was administered at once, followed by an intra-uterine douche of the same solution. My attention having been called to the use of Parke, Davis & Co.'s nuclein in puerperal septicemia, and having had satisfactory results from its use in cases of surgical sepsis, I ordered one

drachm of the five-per-cent. nuclein solution (P., D. & Co.'s) to be given internally every three hours. The day following the nurse in charge of the case reported a slight chill followed by a temperature of 105°, pulse 110, but general condition of patient somewhat improved.

Vaginal douches were given daily by the nurse, and nuclein continued as before. No recurrence of the chills occurred after the second day. The temperature remained approximately the same for six days, when it fell by crisis. Although during the first six days there was very little variation in the height of the temperature, the daily remissions were marked, and the pulse continued to fall steadily and improve in quality, the general condition being one of progression. The patient's mental condition changed rapidly for the better, appetite returned, and the skin assumed its normal color.

Nuclein, then, is a remedy which aids us in fulfilling the second indication in the treatment of puerperal septicemia—*i. e.*, the strengthening of Nature's antitoxic [or germicidal] elements. It acts favorably and promptly upon leucocytosis, it causes no unpleasant complications or effects, it acts rapidly, and under its use the fetid discharges quickly diminish.

In Scrofula.

Oscar R. Tomlinson, M.D., of the New York Infant Asylum, Mt. Vernon, N. Y., makes the following report on his experience with nuclein solution in the treatment of scrofula (*Journal of the American Medical Association*, Sept. 4, 1897):

Case 1.—O. V. Muco-purulent discharge from nose and ears. Gums and the mucous membrane of the mouth in an unhealthy condition and bleed for the slightest irritation. Chronic conjunctivitis. Very irritable. Large head; protruding abdomen. All the usual symptoms of rachitis. Began the administration of nuclein solution April 9: $\frac{1}{2}$ drachm three times a day, before eating. Temperature normal or not above 99° until May 1, when I increased the dose to $1\frac{1}{2}$ drachms (I began to give 1 drachm on April 24, which made little impres-

sion). The child began to improve in appearance by May 5, and on May 19 was well and all the disagreeable symptoms and complications had disappeared.

Case 2.—W. H. Weak, pale, and fretful infant, extremely nervous and irritable. Enlarged lymphatic glands, large head, and protruding abdomen. Discharge from nose and ears. Began treatment April 9, and it is being continued at this writing (May 22). The case has improved very much in every respect. All discharges have stopped, the formerly enlarged glands are no longer noticeable, and I confidently expect a complete restoration to health in a short time.

Case 3.—A. L. Phlegmatic temperament. About the same condition as Case 2. Enlarged glands, decayed teeth, discharge from nostrils. All disagreeable symptoms have almost entirely disappeared at this time.

Case 4.—C. M. Discharge from nose and ears; enlarged glands. Nervous temperament. Condition very similar to that of Case 1. This case is now well and the treatment discontinued.

Case 5.—E. K.—, female, aged three years. Had bronchopneumonia, which was followed by whooping-cough; then chronic bronchitis; then there was another attack of bronchopneumonia followed by a foul-smelling discharge from the right nostril and right ear. Bleeding gums. Restless and irritable. I began the treatment by administering half a drachm of nuclein, but soon increased the dose to one and a half drachms, which produced only a slight rise in temperature; but the child improved rapidly. For a week after the treatment was begun the discharge from the ear and the nostril was largely increased in quantity, and the odor of the discharge also appeared to be increased. After the first week the discharge gradually diminished, first in odor and then in quantity. The child became bright and playful, and finally the nostril healed; there had been so much loss of tissue that the healing process almost closed the opening. The ear healed also. The lung symptoms disappeared, and within five weeks from the beginning of the nuclein treatment the child was *apparently perfectly well.*

Case 6.—N. R——, female, aged two years and six months; listless, emaciated; chronic eczema, with boils in various parts of the body. Discharge from left ear. Nuclein, one drachm, was given three times a day, and all of the symptoms, including the eczema, disappeared and the child became energetic and playful. I do not attempt to account for the relief of the eczema from the administration of the nuclein, but it certainly disappeared with the other complications after only three weeks' treatment.

Case 7.—A. K——, female, aged ten months. The submaxillary glands were swollen, were large and sensitive to the touch, and it appeared as if they were on the verge of suppuration; but within a few days after the nuclein treatment was begun the glands began to subside, and after four weeks' treatment the child was entirely well.

Case 8.—L. H——, female, aged one year. A typical case of "scrofula." One of the glands was already suppurating when I began the treatment. Immediately after two more glands broke down and there were large quantities of pus thrown off. The suppurative process appeared to be hastened for a time, but within six weeks from the beginning of treatment there was no evidence of the disease remaining.

Case 9.—A. H——, female, aged eight months. Another case of "scrofula." Two glands were discharging. Soon after the administration of nuclein was begun the discharge disappeared, and after three weeks' treatment the patient was discharged cured.

I fully appreciate the difficulties involved in the treatment of cases of this character with nuclein solution, but I feel that I can urge upon the profession the importance of the remedy and that it is worth while in the chronic ailments of children of the character described to undertake the treatment; but being careful to caution the parents or guardian of the child that the treatment must be carried on systematically and for some weeks, and that the case must be examined from time to time and the dose carefully increased if necessary, and temperature and weight noted, even if it is not convenient to have a blood count made. Nuclein solution cannot be used

successfully if it is prescribed offhand and the parents allowed to regulate the treatment without reference to the conditions above named. I am also fully convinced that most clinicians who have prescribed this nuclein solution have given it in too small a dose. I found that even young infants could take, with advantage, as much as two teaspoonfuls three times a day, and if a less dose had been given the treatment would not have been successful. I found that young children take the nuclein solution more readily if the proper dose is mixed with a little sweetened water.

J. Ivimey Dowling, M.D., of New York, writes to the *Medical Times* for April, 1897:

Some clinicians claim that scrofula is a tubercular manifestation of the lymphatic system, others that it is a dyscrasia independent of tuberculosis, but the weight of evidence appears to favor the first proposition, as bacteriologists have found tubercle bacilli in glands diagnosed as scrofulous, and therefore consider it an early and curable stage of tuberculosis.

It is well known that the cervical, inguinal, bronchial and mesenteric glands are most often diseased, but other glands may be involved.

Throughout this paper the term "scrofulosis" indicates a condition characterized by enlargement of the lymphatic glands; transparent, delicate skin through which the veins are readily distinguished; the eyes generally bright and the sclera of a bluish tint. The features may be coarse or delicate, the flesh firm or flabby. The abdomen is, as a rule, large and protruding. Differences in temperament are accompanied by certain groups of symptoms which render possible the classification into nervous and phlegmatic types.

The tendency of scrofulous glands is to cheesy degeneration and finally suppuration. It is in the province of treatment to prevent either of these progressions, for the cheesy glands make a favorable nidus for the tubercle bacillus, and the suppurating scrofulous gland is prone to become a tedious charge

to the patient, finally healing, but leaving as a legacy a most unsightly scar.

Surgical treatment is to be deplored nearly as much as allowing the glands to suppurate, for the excision of the glands does not eliminate or render latent the diathesis, and leaves a scar which is undesirable even though it be a linear one and proof of the surgeon's skill.

Hygienic and remedial measures, used conjointly, yield the best results.

It has been my privilege to test the efficiency of nuclein solution, 5-per-cent. (Parke, Davis & Co.), in these conditions.

The first cases in which I tested the remedy were two boys, and their improvement was so marked that it was decided to pursue investigations still further, and accordingly two girls were chosen for treatment from among the 350 children of the Five Points House of Industry.

Case 1.—Campbell C—, aged seven. Head well shaped, $20\frac{1}{2}$ inches in circumference, covered with dark fine hair. Muscles firm, but abdomen slightly protuberant. Cervical glands the size of pigeon's eggs; inguinal glands slightly enlarged. Patient active and of nervous temperament.

After twenty days' treatment with nucleinic acid, one drachm thrice daily, taken orally before meals, his condition apparently was not materially changed. So I increased the dose to two drachms, and within one week there was marked improvement in the general condition, but particularly in the glandular enlargements; the cervical glands had diminished fully one-third in size. These beneficial effects continued, and on November 19, 1896, he was discharged from the hospital. He was under treatment for about twenty-five days before any decided change was observed. It is now over three months since the subsidence of symptoms, and there is no apparent tendency to a return of similar manifestations; consequently, in his case, I consider the remedy to have worked marked curative effects.

Case 2.—James F—, aged seven, was the second patient to receive the preparation, and he passed through similar but longer stages before a cure was effected. He presented the

pathognomonic symptoms noted in Case 1. Head well shaped and $19\frac{3}{4}$ inches in circumference; "pigeon breast;" protruding abdomen and flabby muscles. Patient slow in action, and also mentally sluggish. "Phlegmatic" describes his entire being.

Beginning with one drachm of the remedy, I increased the dose to $1\frac{1}{2}$ drachms on the twentieth day, when a slow improvement began, but in the hope of hastening the progress the dose was again increased, three weeks later, to two drachms. This larger dose caused the glands and tissues of the affected side to become somewhat swollen and tender, but this condition only continued for a few days, after which a rapid subsidence of symptoms occurred, and in the course of ten days more the medicine was discontinued, the boy being cured of his scrofulous glandular manifestations. The inguinal glands disappeared as well as the cervical.

The benefits in this case were not as rapid as in Case 1, but I attribute this to the difference in temperaments, the first being nervous and the other phlegmatic.

Case 3.—Louise B—, aged 12. Head well-rounded, measuring 21 inches in circumference. Same group of symptoms as Case 2.

On November 19, 1896, she received an initial dose of one drachm, which was continued thrice daily for three weeks, when it was increased to two drachms, as there had been no improvement under the smaller dose. Up to the present time, February 25, 1897, there has been no decided benefit, although her appetite is much better and the glands are evidently somewhat reduced in size.

In this patient there has been *no rise of temperature at any time which could be attributed to the nuclein*. This is probably due to her phlegmatic temperament, so I will increase the dose to $2\frac{1}{2}$ drachms.

Case 4.—Viola T—, aged four. The head measures $18\frac{3}{4}$ inches. Cervical glands greatly enlarged, on the left side as large as hen's eggs. In the inguinal region, shotty enlargement of glands. Abdomen rather large. Patient quick in action and mentally bright, distinctly of a nervous temperament.

She received a first dose of one drachm, t. i. d. At the end of the first week there was a noticeable decrease in the size of the lymphatic enlargements, with general constitutional improvement, which was more marked than in any previous case and continued until December 16, 1896, when she was stricken with scarlet fever. The nuclein was now discontinued, and attention paid to the acute malady, from which she made a good recovery, except for marked weakness. On February 5 1897, the remedy was resumed, the glands having remained stationary during the fever. At the time of returning to nuclein the glands were about two-thirds of the original size. From then until the cure, one drachm thrice daily was administered. The benefit was marked and rapid, the weakness which was left by scarlet fever soon disappeared, and no rise in temperature was apparent. The decided gain in strength indicates a tonic action of the remedy.

In Hip-joint Disease.

Another most beneficial agent incorporated in the armamentarium of the surgeon for the treatment of this condition, is Vaughan's nuclein solution as produced by Parke, Davis & Co. I have used it in conjunction with extension in a number of cases. In one case, that of a man aged 44 years, I gave the five-per-cent. solution by the mouth in rapidly increasing doses, until he was taking 60 minims four times daily. From the very beginning an attempt was made to thoroughly saturate him with the nuclein, and the happy results more than repaid us. A rapid decrease in the swelling about the hip-joint took place, the tenderness wholly disappeared, his appetite improved, and there was a complete subsidence of the usual train of annoying symptoms, that rarely, in previous cases, had been accomplished by extension alone. During the incarceration of this patient's hip-joint, he gained over twenty pounds in weight. He had previously undergone amputation of the foot, on the same leg that now suffered from hip disease, for tuberculosis of the ankle. At the time the extension apparatus was adjusted there were several small tubercular ulcers on the tibia above

the stump; hence it was not without misgivings that radical treatment was instituted. And I feel compelled to admit that without such a powerful agent as Vaughan's nuclein solution, producing a vigorous leucocytosis, the result in this case could not have been good. The great increase in the disease-resisting power afforded the human body by such an element, its germicidal influence and antiseptic properties, recommend it very strongly to our consideration in these cases. Experimenters speak of it very highly also in cases of mixed infection. Its use, either by mouth or hypodermatically, is attended by no evil results. I presume I have given nearly 1000 injections of it, and have had as yet no needle abscess—something one cannot say of all the various antitoxins we use nowadays.—CHAS. G. PLUMMER, B.S., M.D., in the *Journal of the American Medical Association*, Feb. 25, 1899.

In Malignant Disease.

Case 1.—The first of June, 1894, Mr. S., aged 55, consulted me as to a small tumor on the right cheek, one and a half inches beneath the orbit; the growth was about three-eighths of an inch in diameter, presenting the appearance of epithelioma. I at once pronounced it malignant, and advised removal. The patient, however, sought the opinion of another physician, and was advised not to allow an operation, as it was "only a skin disease." Tincture of iodine, peroxide of hydrogen, and ointments were prescribed, yet within a few weeks the tumor rapidly increased in size, ulcerated, and became very painful. The growth was removed by the family physician in October, and was then one and a half inches in diameter. Return was rapid and ulceration destructive. A second operation was performed after an interval of a few months, but this, like the first, was not sufficiently radical; now the whole wound became involved and destructive growth rapid. Here the cancer quack got hold of the case, and salves, pastes and oils were tried, one and another, until the case became desperate. I saw Mr. S. the second time on June 22, 1895, and then deemed the case hopeless; the cavity of the

ulcer was three inches in diameter, had destroyed the infra-orbital arch and the zygomatic arch to its articulation with the temporal bone, and even entered the antrum and orbit, the dead and decaying bone and flesh producing a stench terrible to endure. The lymphatic glands of the neck and groin were swollen and tender; skin dry and harsh; patient very feeble, much reduced in flesh, having night-sweats and hectic; the discharge was so profuse that dressings had to be changed many times during each day. My attention having been called to the action of nuclein in epithelioma, by Professor Robinson, of New York, I decided to try it, employing as an external dressing only carbolized vaselin. June 22, 1895, I began with ten minims, injecting into the arm, shoulders, and back. Increased gradually to twenty drops each day, when fever and nausea followed by diarrhea set in, which, however, was remedied by two days' rest. Next I increased to thirty minims—diarrhea, nausea and fever following. Again two days' rest; then thirty to forty drops each day as long as treatment was continued.

There was a gain in flesh of one and a half pounds during the first ten days of treatment. Appetite increased, strength improved, sweating ceased, skin became softer and smooth, pain very much relieved, and sleep better; the swelling was much reduced, ulcer looking more healthy, with but little discharge and that not so offensive, and where the diseased tissue sloughed away the flesh looked healthy and clean; granulations sprang up in many parts of ulcer, and at inner angle of eye, uniting and closing in the ulcerated surface. Improvement continued for four weeks, as shown by smaller size of tumor, sloughing away of dead bone without further destruction, and closing up of ulcer to two and a half inches in diameter, when it required to be dressed but once a day. There was general arrest of disease process except in antrum and nose. Swelling of glands disappeared at the end of four weeks, and now the improvement was so noticeable that friends on the streets pronounced a cure being made. Nervous complications developed; the knowledge of the progress of the disease, seemingly going on unchecked in the nose and

antrum, disheartened Mr. S., and he became despondent and hopeless, and finally decided to return home to die, which he did. He lived about two months longer, but never got into the extremely loathsome condition he presented when I first began treatment, and he suffered much less pain.

Had this case been treated with nuclein six months earlier, I believe it would have recovered.

Case 2.—Mrs. M., aged 56, came to me October 1, 1895. She was a large and apparently well nourished woman, though very nervous, restless, and feeble. Little was learned of her family history. A distant relative had died of cancer, and one of lung disease. The right eye was pushed forward about one-fourth inch beyond normal, and slightly outward; sight almost destroyed, and but slight movement of eyeball. At the inner angle, deep down in the orbit, could be felt a tumor the size of a fibert, hard and fixed and resistant to touch. Between the eyeball and lower lid a soft tumor, one and a half inches by half an inch, adhered to the sclera up to the corneal junction, entirely covering the lower lid; it was irritable and bleeding. This disease was first observed about eighteen months previously. Severe pain in eye, over right temple, in nose and cheek, and over the eye, had been constant symptoms; there was severe pain also in upper teeth of right side. Pulse 100; temperature normal.

I deemed this a case of carcinoma. Nuclein was given by the mouth in ten-drop doses three times a day from October 8 to November 5, then hypodermatically one week, and by mouth to December 1. There was slight fever, restlessness and general constitutional disturbance during first month under treatment, but the tumor was rapidly reduced, pain relieved, and there was general improvement in health, that has continued to the present time. The supply of nuclein was exhausted December 1, and none has been given since. Patient was put on arsenic at this date, and is now taking three to five drops of Fowler's solution thrice daily. Nuclein was ordered for subsequent treatment, but the supply was lost by freezing.

It is my opinion that, if a cure is not made, much good will

result from the administration of this medicament; and this opinion is coincided in by Dr. Woodyard, who saw the case with me and has constantly had it in charge.—T. W. WHITLOCK, M.D., Jonesboro, Tennessee, in *Medical Age*, March 25, 1896.

In a case pronounced a sarcoma by eminent specialists, nucleinic acid apparently wrought a marvelous cure. The patient, wife of a prominent physician on the Pacific Coast, was brought to her home near Ann Arbor in February, 1895, with what was pronounced a sarcoma of the pelvis. She was greatly emaciated, weighed but 75 pounds, and was unable to sit up. There was a hard tumor, round and (as correctly as I could estimate) three inches in diameter, easily felt through the vagina, and apparently growing out from the ilium on the left side. The 1-per-cent. solution of nucleinic acid was employed in the treatment, which was administered by her husband. At first the injections were made directly into the growth through the walls of the vagina by means of a specially prepared needle. Later the injections were made into the gluteal muscles. Treatment was given daily for six months, and then less frequently for some months longer. The strength and weight of the patient gradually increased, and the size of the growth diminished *pari passu*. By the first of July, 1895, the patient weighed more than ever before and was able to walk several blocks. Her husband writes me: "In January, 1896, there was some pain in the left side of the pelvis, and a small hardened mass appeared, quite tender and apparently occupying a fold of the broad ligament. Nuclein was used for about two months, injected into the gluteal region. By May there was no sign of the trouble, and an increase of weight was noticed, as well as an improvement of the general condition. At present writing (Oct. 30, 1896) she weighs 123 pounds, which is about 10 pounds more than she ever weighed before. She is in good spirits and able to perform ordinary duties." Of course this growth might not have been a sarcoma. The fact that it disappeared so completely is presumptive proof that it was not a malignant growth.

but in a similar case I should certainly try the nuclein again.—
Dr. VAUGHAN, in *Medical News*.

I have found a wash of nucleinic acid beneficial in epithelioma, destroying the germs which produced a most disagreeable stench. For this purpose I can commend a 5- or 10-percent. solution as a wash for the diseased surface.—VAUGHAN.

In Diphtheroid Conditions.

Dr. J. M. Bleyer, in the *Medical Record*, reports having treated with nuclein thirty-five cases of follicular tonsillitis and eight cases of pseudo-diphtheria. The nuclein employed was from the laboratory of Parke, Davis & Co. While angina lacunaris follicularis—a disease in which the surface of the tonsils and fauces is inflamed, and stippled with curdy-white or ash-gray points—is not often fatal if properly dealt with, we are reminded by Hamilton that “many instances of diphtheria commence as angina lacunaris,” and that all marked forms of the latter condition are to be regarded as diphtheritic. In these cases fifteen to twenty minims of nuclein hypodermatically administered twice in one day, the injections being given twelve hours apart, were followed by a most remarkable result within twenty hours in every case. No other remedy was employed, excepting gargles or douches of salt water to remove the loose debris lying about the mouth and throat. Slight rise of temperature sometimes followed the injections, rarely as much as three degrees Fahrenheit. All the symptoms usually found subsided within the first twenty-four hours. Some fever remained for thirty-five hours. Nuclein, remarks the author, seems to possess with all its specific action another advantage—that of a dynamogenetic power, increasing the vigor of the central nervous system.

In that type known to us as pseudo-diphtheria the same promptness of action was noticeable, with the one exception that a longer time was needed for complete recovery (three or

four days). In these patients the injections were given every eight hours, in doses of twenty minims, and the salt-water irrigations were applied every hour. All of the eight patients recovered within four days.

The earlier in the disease the nuclein is administered, the better. When the injection is well driven into the muscular or subcutaneous tissue it is not painful, though local numbness is sometimes experienced. Nuclein is absorbed in a few moments. In no case is there found to be any local reaction if antisepsis has been carried out.

Bleyer concludes from his own experience that nuclein is a staunch medicament and one that will undoubtedly prove of great value.

Dr. G. W. Greenleaf, Somerville, Mass., narrates a case of membranous laryngitis which progressed favorably under general treatment until the morning of the fourth day, when sudden collapse became imminent. No emesis followed repeated doses of cupric sulphate, turpeth mineral, and ipecac. Atropine, strychnine and brandy were administered subcutaneously with little good. Fifteen minims of nuclein was then injected into the thigh; a half-hour later, twenty minims, and this last dose repeated every hour. After the first dose, ipecac was repeated and emesis followed; the cyanosis disappeared, and within twenty-four hours the pulse was stronger and regular. Dr. Greenleaf declares himself satisfied as to the efficiency of nuclein in this case, and will henceforth use it from the outset of an attack.—*Therapeutic Notes*, October, 1895.

In Lupoid Ulcer.

Rush McNair, M.D., of Kalamazoo, Mich., narrates (*Medical Summary*) a case in which all manner of persevering treatment proved utterly futile until he resorted to nuclein. Sixty minims were injected daily. A new point for injection was each time chosen, the periphery of the ulcerated area

being thus gradually traversed. The lapse of ten days showed marked local and constitutional improvement. By the end of a full month the cure was radical. Patient is now performing heavy manual labor.

In Syphilitic and Other Diseases.

I have now been using nuclein for sixty days in three different cases—syphilitic anemia, tubercular glands of neck, malarial intoxication with resulting anemia.

Case 1.—The rigorous anti-syphilitic treatment during the past eighteen months, *plus* the syphilis, had rendered the patient almost malignantly anemic. The various stimulating tonics proved futile. Having thoroughly acquainted myself with the literature on nuclein, I obtained a supply through Stern Bros., chemists, and followed in every detail the method of administration directed by Professor Vaughan, with especial reference to strict asepsis in the injections. At the end of sixty days my patient has entirely regained his normal condition; sleeps well, has gained some twenty pounds, and declares he "never felt better in his life!"

Case 2.—The glands of the neck were so profoundly affected as to render surgical interference impossible. My associate, Dr. Grimm, was struck with the great amount of destruction manifested. I refrain from enumerating the familiar collateral symptoms.

As a result of 100 injections, the appetite has returned to normal; 14 pounds have been added to the weight; the cachexia has disappeared; glandular lesions are vanishing. In fact, the sum total of present conditions is a new individual.

Case 3.—Mrs. ——, of Louisiana; enlarged spleen, malarial cachexia, general anemia, basic heart murmur, poor appetite, and digestive disturbances. Iron, digitalis, strychnine, malt preparations, were tried without avail. I began using nuclein, and after twenty injections her cachexia has almost disappeared; appetite has returned, with a gain of seven pounds *in flesh*.

These three cases have impressed me very deeply with a sense of the boon humanity has received in nuclein. I hope the manufacturers will continue to supply such a prize.—R. D. JOHNSON, M.D., San Francisco, Cal., in *Therapeutic Notes*, October, 1895.

A troublesome sinus had been caused by a sloughing tendon leading from the second finger high into the palm of the hand. The patient had suffered a phlegmonous cellulitis of the finger and palm, and there had been free incisions into both. A sinus connected the two openings, and, notwithstanding thorough irrigation with bichloride solutions and with peroxide of hydrogen, it continued to discharge freely. It seemed necessary to extend the cut from the palm down into the finger. Before doing this, however, the thought occurred to throw a solution of nuclein into the sinus. This was done, and, much to my surprise and pleasure, it stopped at once and permanently the purulent discharge. I have since had no opportunity to test its further value in this class of cases, but my experience here will certainly lead me to give it further trial.

A maiden lady aged 39, teacher by occupation, had long been under treatment for neurasthenia. An attempt had been made to carry out the Weir Mitchell treatment in her home, but with indifferent success. She was having daily massage and electricity, together with the prescribed diet. There had been some gain, but much trouble was experienced from flatulent disturbances of the stomach and bowels. The patient was placed on 20-minim doses of nuclein (P., D. & Co.). Under its administration, with the other treatment unchanged, there was a marked improvement in the condition of digestion. The patient made a more rapid and marked gain in other ways as well, so that she was by the end of a month able to ride out for two or three hours and to walk many blocks, something she had not done for over a year. The psychical element in this case may play an important rôle, and, indeed, the nuclein was resorted to largely for the moral effect of a daily hypodermic injection; yet it is my belief that the nuclein was

a real therapeutic element in the case, and this belief is shared by the nurse in attendance, who is a woman of much experience and good training.—FRANK W. GARBER, B.S., M.D., in *Therapeutic Gazette.*

Charles B. Reed, of Chicago, in *Medicine*, December, 1895, reports three cases treated with yeast nuclein. It could hardly have been expected that a cure would have been effected in any of these cases, which were, respectively: diabetes; leukemia with various complications, among the rest a tumor extending from the median line to three centimeters to the right of the umbilicus, its lower border continuous with the pelvis, its upper border extending to the fourth interspace and displacing the apex beat upward and outward; the third case was one of chronic rheumatism. In none of these cases was there any increase of temperature that could be traced to the nuclein. At irregular intervals the dose was abruptly doubled, with no deleterious results. Out of the total of nearly 250 injections, there was but one instance of local inflammation caused by the needle. In Case 1 the occurrence of multiple furuncles ceased when the injections were begun, and those present gradually healed. This can probably be attributed to the nuclein, as the patient had been on anti-diabetic diet for over three months before the nuclein treatment was begun. Under nuclein he began to feel better, appetite and sleep improved; but when full diet was resumed and the nuclein continued, the amount of urine passed was doubled and the amount of sugar trebled. In Case 2 the subjective symptoms improved, the pain ceased, morphine was discontinued except at long intervals, and the patient ate, slept and felt better, but otherwise the course of the disease was unaltered and the size of the tumor mass remained undiminished.

The author concludes:

1. That nuclein is non-toxic.
2. That it is a substance capable of increasing the vital energies of the body.
3. That it is easily assimilated, and physiological in its action.

In a paper read by Dr. R. H. Hayes, of Union Springs, Ala., before the Tri-State Medical Society of Alabama, Georgia, and Tennessee, on "The Nucleins and their Relation to Serotherapy," the writer concludes a very thorough discussion of the subject with the following passage: "Like Dr. Vaughan, who, with his large and scientific experience, was encouraged to continue its use, can also say that I am encouraged from my very limited experience to continue the use of the nucleins, and feel no fear of dangerous results, at least from the yeast nuclein solution. These remedies have already won place and position in practical therapeutics, and the universally favorable reports from clinicians of ability and repute give them prestige greater than that won by any other class of remedies during the past two decades. It seems to me to presage the passing of many of the older orthodox remedies, and that the nucleins, unlike ordinary fads or some of the proprietary innovations, have come to stay."

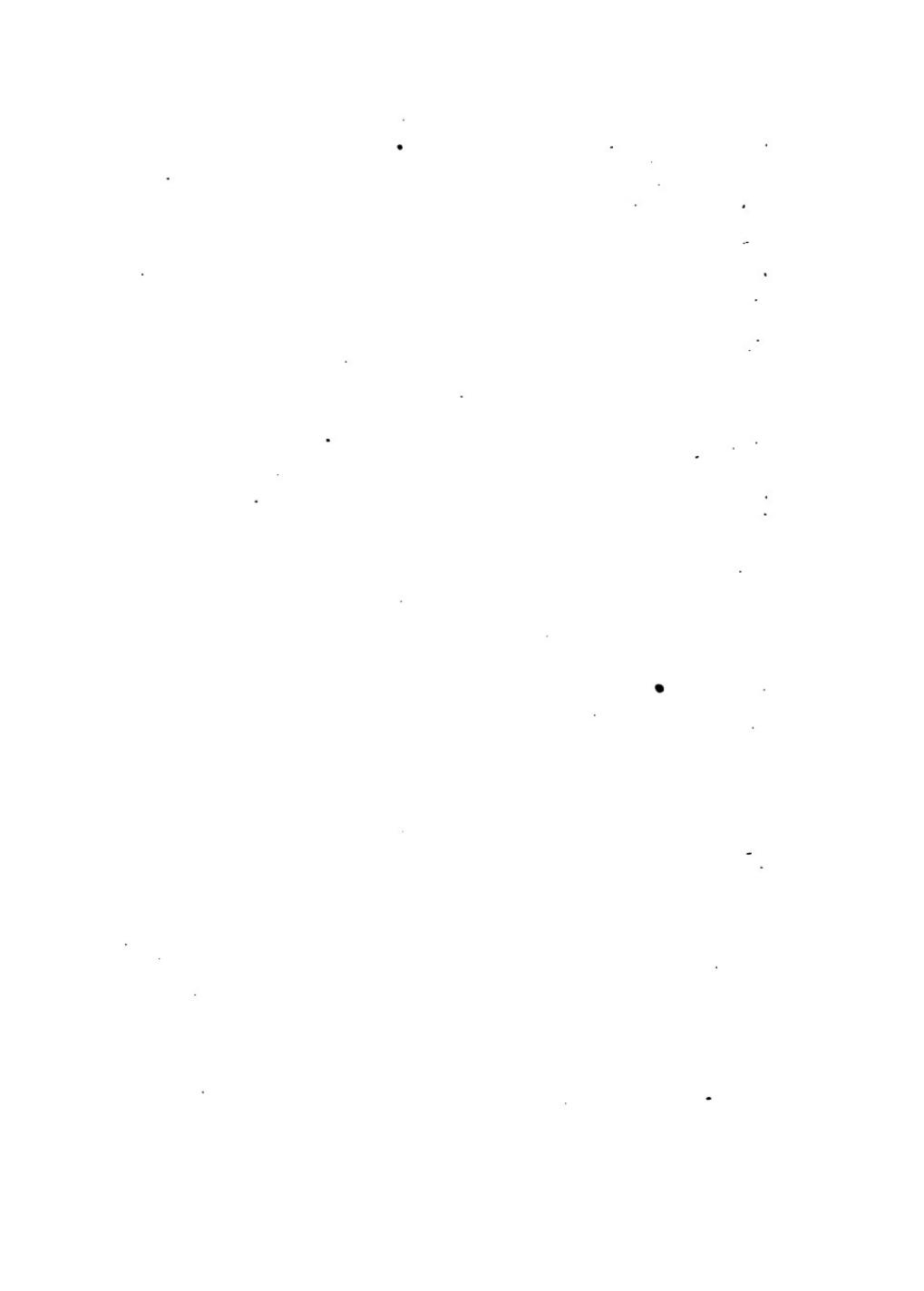
Dr. E. A. Johnston, Henrietta, Texas, writes: "I am meeting with unprecedented success in the administration of your nuclein solution in various disorders. I have just dismissed a bad case of diphtheria cured with three injections of 10, 15, and 20 drops. I cannot practice medicine without your nuclein solution."

I have repeatedly tested this agent in pneumonia, pleuritis, and other inflammatory and infectious diseases, with most satisfactory results. Even in three cases of alcoholic and albuminuric pneumonia a manifestly favorable influence was exerted.—GERMAIN SÉE.

Yeast nucleinic acid has a markedly retarding effect upon fermentation in the small intestines, as we have shown by determining its influence upon the conjugate acids eliminated in the urine.—VAUGHAN.

Parke, Davis & Co. have introduced a solution of nuclein adapted to administration by the mouth. A sample has been submitted to us. It is a brownish fluid, with a slight smell of carbolic acid which is more noticeable on heating, an acid reaction equal to 0.12 per cent. HCl, and is not unpleasant to taste. Analysis shows, . . . after reducing the nucleinic acid present to its base, hypoxanthin, 0.355 per cent. of a derivative. . . . This solution of nuclein is prepared from yeast, and is said to contain 5 per cent. of nucleinic acid, a statement confirmed by the quantity of hypoxanthin recovered from it.—*Edinburgh Medical Journal*, March, 1897.







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